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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/560,357

12/12/2005

Hiroshi Tomiyama

TAN-356

8894

7590 02/29/2008
H. Jay Spiegel and Associates PC
P.O. Box 11
Mount Vernon, VA 22121

EXAMINER

BLAND, LAYLA D

ART UNIT	PAPER NUMBER
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1623

MAIL DATE	DELIVERY MODE
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02/29/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,357	TOMIYAMA ET AL.	
	Examiner	Art Unit	
	LAYLA BLAND	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 January 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 3,7,8,10,12,14,17 and 20-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-6, 9, 11, 13, 15, 16, 18, 19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>4/25/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Priority

This application is a national stage entry of International Application No. PCT/JP04/08678, filed June 15, 2004, which claims foreign priority to Japanese Application No. 2003-185171, filed on June 27, 2003 under 35 U.S.C. 119(a)-(d). The copy of certified copy of the priority has been filed with the instant Application. It is noted that Japanese Application No. 2003-185171 is in Japanese; no translation of said Japanese application into English has been provided.

Applicant's election without traverse of Group I in the reply filed on January 11, 2008 is acknowledged. In the restriction requirement dated December 11, 2007, claims 10, 12, 14, 17, and 20 were erroneously included in Group I. These claims depend from non-elected claim 3 and are withdrawn from consideration.

Claims 1-28 are pending in this application. Claims 3, 7, 8, 10, 12, 14, 17, and 20-28 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1, 2, 4-6, 9, 11, 13, 15, 16, 18, and 19 are examined on the merits herein.

Claim Objections

Claim 2 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. The claims differ in the use of the word "combination" versus the word "mixture." When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is

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proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). (It is noted that the claims are not allowed at this time)

It is also noted that several of the other pending claims may be duplicates of each other. Applicant is encouraged to review the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-6, 9, 11, 13, 15, 16, 18, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

Claim 4 is drawn to the agent of claim one and consists of a compound of the given formula. The agent of claim 1 consists of both a compound of formula (I) and a cholesterol biosynthesis inhibitor. There is a lack of antecedent basis for this limitation in the claim; the agent cannot consist of a combination of a compound of formula (I) and a cholesterol biosynthesis inhibitor and also consist of only a compound of the given formula. "Consisting of" is closed language which does not permit the inclusion of any other elements into the composition. Claims 5, 9, and 11 are similarly rejected.

Claim 6 is drawn to the agent of claim 1 "characterized by the use of" specific types of cholesterol biosynthesis inhibitors. Claim 1 is a product claim and it is unclear what is meant by "use." The claim is interpreted to mean that at least one cholesterol biosynthesis inhibitor must be present in the composition of claim 1 and must be a HMG-CoA reductase inhibitor, squalene synthase inhibitor, or squalene epoxidase inhibitor. Similarly, claims 13, 15, 16, 18, and 19 are rejected. Clarification is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

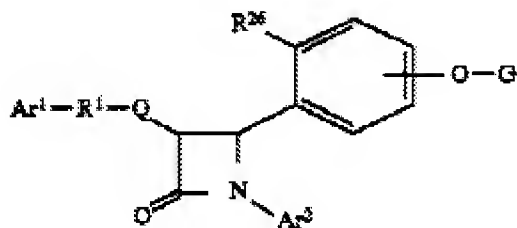
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 4-6, 9, 11, 13, 15, 16, 18, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yumibe et al. (US 5,756,470, May 26, 1998) and Tomiyama et al. (US 2004/0063929, April 1, 2004, PTO-1449 submitted April 25, 2006, English equivalent of WO02/066464, published August 29, 2002).

Yumibe et al. teaches a combination of a cholesterol biosynthesis inhibitor and a β -lactam cholesterol absorption inhibitor for lowering cholesterol and treating or preventing atherosclerosis [see abstract]. The combination of a beta-lactam cholesterol absorption inhibitor and HMG CoA reductase inhibitor results in a greater decrease in plasma cholesterol than either agent alone [column 2, lines 11-20]. Suitable cholesterol

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biosynthesis inhibitors include HMG CoA reductase inhibitors, squalene synthesis inhibitors, and squalene epoxidase inhibitors [column 2, lines 51-63 and claim 20]. The genus of compounds taught by Yumibe et al. is as follows [column 2]:



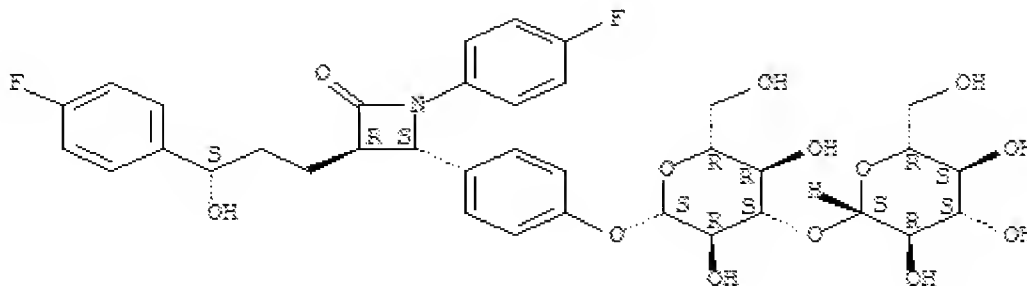
Wherein R^{26} is H or O-sugar, G is a sugar, and Ar^1 and Ar^2 are aryl or substituted aryl. Specific embodiments are claimed in claim 13 and include, among others, the following:

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L2  ANSWER 3 OF 45  REGISTRY  COPYRIGHT 2008 ACS on STN
RN  208259-77-2  REGISTRY
ED  Entered SIN:  09 Jul 1998
CN  2-Azetidinone, 1-(4-fluorophenyl)-3-[(3S)-3-(4-fluorophenyl)-3-
hydroxypropyl]-4-[4-[(3-O-β-D-glucopyranosyl-β-D-
glucopyranosyl)oxy]phenyl]-, (3R,4S)-  (CA INDEX NAME)
FS  STEREOSEARCH
MF  C36 H41 F2 N O13
SR  CA
LC  STN Files:  CA, CAPLUS, USPATFULL

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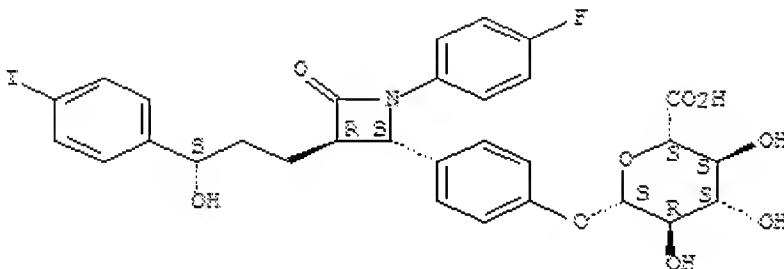
Absolute stereochemistry.



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L2 ANSWER 11 OF 45 REGISTRY COPYRIGHT 2008 ACS on STN
 RM 150448-79-4 REGISTRY
 ED Entered SIN: 27 Jun 1997
 CN β -D-Glucopyranosiduronic acid, 4-[(2S,3R)-1-(4-fluorophenyl)-3-[(3S)-3-hydroxy-3-(4-iodophenyl)propyl]-4-oxo-2-azetidinyl]phenyl [CA INDEX NAME]
 FS STEREOSEARCH
 MF C30 H29 F I N O9
 BR CA
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



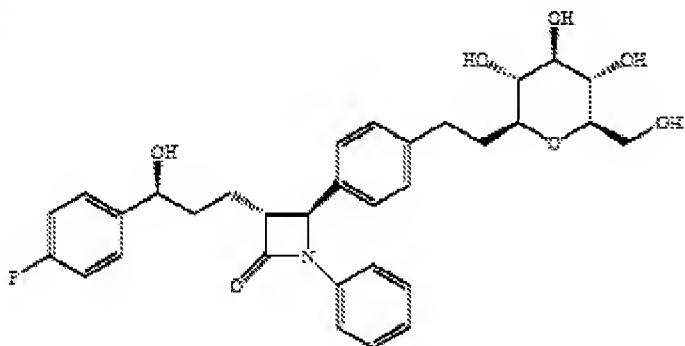
The difference in the beta-lactams taught by Yumibe et al. and the instantly claimed beta-lactams is that the instantly claimed lactams comprise C-glycosides and those of Yumibe et al. comprise O-glycosides.

Tomiyaama et al. teach beta-lactam compounds which are useful as serum cholesterol-lowering agents and which meet the limitations of the instant claims [see abstract and columns 2-3, and structures in columns 7-36]. Tomiyaama et al. teach that O-glycoside bonds in beta-lactam-O-glucuronate compounds can be hydrolyzed in the small intestine, possibly reducing the activity of the compounds [column 1, lines 51-62]. Beta-lactams having a C-glycoside, which is stable to metabolism by glycosidase and hydrolysis, were prepared [column 2, lines 3-10]. One preferred compound, compound

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56 [column 35], shown below, is the same compound as that which is recited in instant claim 4:

56



Other preferred compounds include compound 37 [column 25], which is the same compound as that which is recited in instant claim 5.

Tomiyama et al. do not teach a combination of beta-lactam and cholesterol biosynthesis inhibitor.

It would have been obvious to one of ordinary skill in the art to prepare a cholesterol-lowering composition comprised of a cholesterol biosynthesis inhibitor and a β -lactam taught by Tomiyama et al. The combination of beta-lactam cholesterol absorption inhibitor and cholesterol biosynthesis inhibitor is already known in the art, as taught by Yumibe et al. Tomiyama et al. teach modified beta-lactams which are ideal cholesterol absorption inhibitors with low incidence of side effects [column 1, line 65 - column 2, line 2]. One of ordinary skill in the art could have substituted Tomiyama's modified beta-lactams for the beta-lactams in the combination taught by Yumibe et al. and would have predicted that the resulting composition would be effective for reducing plasma cholesterol levels and treating atherosclerosis.

Further, both cholesterol biosynthesis inhibitors and the β -lactams taught by Tomiyama et al. are known in the art for reducing serum cholesterol levels. It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose. In re Kerkhoven, 626 F.2d 846, 205 U.S.P.Q. 1069 (C.C.P.A. 1980).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on M-F 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Layla Bland/
Examiner, Art Unit 1623

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623